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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,443	08/17/2007	Jaume Pons	PC19492A	4751
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PFIZER INC 10555 SCIENCE CENTER DRIVE SAN DIEGO, CA 92121				
EXAMINER				
GUSLOW, ANNE				
ART UNIT		PAPER NUMBER		
1643				
NOTIFICATION DATE		DELIVERY MODE		
10/14/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

-ipgslaj@pfizer.com

Office Action Summary

Application No.

10/584,443

Applicant(s)

PONS, JAUME

Examiner

ANNE M. GUSSOW

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 July 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5-26 is/are pending in the application.
- 4a) Of the above claim(s) 18-22 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-17, 23, 24 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Claims 5, 6, 9-11, 13, 15, 23, 24, and 26 have been amended.

Claims 1-4 and 27 have been cancelled.

Claims 18-22 and 25 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 3, 2009.

2. Claims 5-17, 23, 24, and 26 are under examination.
3. The following office action contains NEW GROUNDS of Rejection.

Objections Withdrawn

4. The objections to claims 4, 23, and 24 are withdrawn in view of applicant's amendment to the claims.

Rejections Maintained/ NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The rejection of claims 5-17, 23, and 24 under 35 U.S.C. 112, first paragraph, as lacking enablement is maintained. **This is a new rejection of claim 5.**

Applicant's arguments filed July 26, 2010 have been carefully considered by the examiner but they are deemed not to be persuasive. The response states that in order to speed prosecution of these claims, Applicant herein cancels claims 1-4, and amends claims 6-14 such that they depend from claim 5, which recites 6 CDR sequences (see response page 7).

Response to Arguments

In response to this argument, applicant's amendment to claim 5 appears to have duplicated the light chain CDRs in the section of the claim related to the heavy chain CDRs. As claimed, the instant antibody would have 9 CDR regions.

For the reasons set forth in the previous office action, antibodies require a total of 6 (or multiples of 6 for multivalent antibodies) CDR regions to form a functional antigen binding site.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which

maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff, et al. (Proceedings of the National Academy of Sciences, 1982. Vol 79 page 1979, as cited on the PTO-892 mailed March 25, 2010). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

MacCallum, et al. (Journal of Molecular Biology, 1996. Vol. 262, pages 732-745, as cited on the PTO-892 mailed March 25, 2010) analyzed many different antibodies for interactions with antigen and state that although CDR3 of the heavy and light chain dominate, a number of residues outside the standard CDR definitions make antigen contacts (see page 733, right column) and non- contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (see page 735, left column). De Pascalis, et al. (Journal of Immunology, 2002. Vol. 169, pages 3076-3084, as cited on the PTO-892 mailed March 25, 2010) demonstrate that grafting of the CDRs into a human framework was performed by grafting CDR residues and maintaining framework residues that were deemed essential for preserving the structural integrity of the antigen binding site (see page 3079, right column). Although abbreviated CDR residues were used in the constructs, some residues in all 6 CDRs were used for the constructs (see page 3080, left column).

The fact that not just one CDR is essential for antigen binding or maintaining the conformation of the antigen binding site is underscored by Casset, et al. (Biochemical and Biophysical Research Communications, 2003. Vol. 307, pages 198-205, as cited on the PTO-892 mailed March 25, 2010) which constructed a peptide mimetic of an anti-CD4 monoclonal antibody binding site by rational design and the peptide was designed with 27 residues formed by residues from 5 CDRs (see entire document). Casset, et al. also states that although CDR H3 is at the center of most if not all antigen interactions, clearly other CDRs play an important role in the recognition process (page 199, left column) and this is demonstrated in this work by using all CDRs except L2 and additionally using a framework residue located just before the H3 (see page 202, left column). Vajdos, et al. (Journal of Molecular Biology, 2002. Vol. 320, pages 415-428, as cited on the PTO-892 mailed March 25, 2010) additionally state that antigen binding is primarily mediated by the CDRs more highly conserved framework segments which connect the CDRs are mainly involved in supporting the CDR loop conformations and in some cases framework residues also contact antigen (page 416, left column). Holm, et al. (Molecular Immunology, 2007. Vol. 44, pages 1075-1084, as cited on the PTO-892 mailed March 25, 2010) describes the mapping of an anti-cytokeratin antibody where although residues in the CDR3 of the heavy chain were involved in antigen binding unexpectedly a residue in CDR2 of the light chain was also involved (abstract). Chen, et al. (Journal of Molecular Biology, 1999. Vol. 293, pages 865-881, as cited on the PTO-892 mailed March 25, 2010) describe high affinity variant antibodies binding to VEGF wherein the results show that the antigen binding site is almost entirely composed of

residues from heavy chain CDRs, CDR-H1, H2, H3 (page 866). Wu, et al. (Journal of Molecular Biology, 1999. Vol. 294, pages 151-162, as cited on the PTO-892 mailed March 25, 2010) state that it is difficult to predict which framework residues serve a critical role in maintaining affinity and specificity due in part to the large conformational change in antibodies that accompany antigen binding (page 152 left column) but certain residues have been identified as important for maintaining conformation.

There is insufficient evidence or nexus that would lead the skilled artisan to predict the ability to produce a functional antibody comprising fewer than 6 CDR regions. The specification does not teach how to make an antibody that would bind trkC and comprise fewer than 6 CDR regions.

Therefore after a fresh consideration of the claims and the evidence provided the rejection is maintained.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. The rejection of claims 5-16 and 26 under 35 U.S.C. 102(e) as being anticipated by Shelton (WO 2004/058190, priority to December 23, 2002) is maintained.

Applicant's arguments filed July 26, 2010 have been carefully considered by the examiner but they are deemed not to be persuasive. The response states that applicants note that each of these provisional applications disclose only the mouse anti-TrkC antibody 2256 and its sequences and do not disclose the humanized anti-TrkC antibody A5 and its sequences. Therefore, given that the present application claims priority to a US provisional application filed December 23, 2003 (on or before the date of filing of the applications cited in this rejection), and given the claims of the present application exclude antibody 2256 sequences, applicant respectfully requests reconsideration and withdrawal of this rejection (see response pages 7-8).

Response to Arguments

In response to this argument, the reference has a proper 102e date of December 23, 2002 as set forth in MPEP 706.02(a). The reference teaches the antibody may be a humanized antibody, and has CDR sequences that are identical to the instantly claimed CDR sequences. One of ordinary skill in the art would recognize that a humanized antibody would comprise CDR sequences from a non-human antibody and framework and constant regions from a human antibody. Since the claims recite only the specific CDR sequences (not the frameworks or complete antibody heavy or light chain) for the antibody and Shelton teach humanized antibodies comprising the same CDR sequences the instantly claimed antibodies are anticipated by Shelton.

Therefore after a fresh consideration of the claims and the evidence provided the rejection is maintained.

9. The rejection of claims 5-16 and 26 under 35 U.S.C. 102(e) as being anticipated by Shelton (US PG PUB 2007/0014786) is maintained.

Applicant's arguments filed July 26, 2010 have been carefully considered by the examiner but they are deemed not to be persuasive. The response states that applicants note that each of these provisional applications disclose only the mouse anti-TrkC antibody 2256 and its sequences and do not disclose the humanized anti-TrkC antibody A5 and its sequences. Therefore, given that the present application claims priority to a US provisional application filed December 23, 2003 (on or before the date of filing of the applications cited in this rejection), and given the claims of the present application exclude antibody 2256 sequences, applicant respectfully requests reconsideration and withdrawal of this rejection (see response pages 7-8).

Response to Arguments

In response to this argument, the reference has a proper 102e date of March 20, 2003 as set forth in MPEP 706.02(a). The reference teaches the antibody may be a humanized antibody, and has CDR sequences that are identical to the instantly claimed CDR sequences. One of ordinary skill in the art would recognize that a humanized antibody would comprise CDR sequences from a non-human antibody and framework and constant regions from a human antibody. Since the claims recite only the specific CDR sequences (not the frameworks or complete antibody heavy or light chain) for the antibody and Shelton teach humanized antibodies comprising the same CDR sequences the instantly claimed antibodies are anticipated by Shelton.

Therefore after a fresh consideration of the claims and the evidence provided the rejection is maintained.

Conclusion

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is

(571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
October 6, 2010

/Anne M. Gussow/
Examiner, Art Unit 1643

/Misook Yu/
Supervisory Patent Examiner, Art Unit 1643